Regulatory Education for Industry (REdI):
GENERIC DRUGS FORUM

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Amendments to Original ANDAs and PASs Under GDUFA

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Agenda

- GDUFA Goal Information
- Amendments Performance Metrics
- Draft Guidance for Industry, Amendments & ECDs under GDUFA

GDUFA Goal Information

GDUFA Goal Information

- Designed to speed the delivery of safe and effective generic drugs to the public
- Based on an agreement negotiated by FDA and the generic drug industry to address regulatory challenges
- Performance goals include the review of amendments submitted electronically to original ANDAs and PASs submitted electronically on or after October 1, 2014

GDUFA Goal Information

- **GDUFA goals apply to electronic submissions made on or after 10/1/14 of:**
  - **original ANDAs**
  - **PASs**
  - **amendments to original ANDAs submitted electronically on or after 10/1/14**
  - **amendments to PASs submitted electronically on or after 10/1/14**
- **An ANDA is assigned a cohort year based on the FY in which it was first submitted**

Amendments Performance Metrics

Amendment Performance Metrics Basics

- **GDUFA Commitment Letter identifies review goals for amendments to ANDAs and PASs**
- **All amendment goal dates are incremental and calculated from the date of electronic submission**
  - **An amendment pre-CR letter adjusts the goal date**
  - **An amendment post-CR letter sets a new goal date**
- **Amendments never shorten the ANDA goal date**
- **If an amendment contains multiple elements – longest goal date applies**

GDUFA Amendment Terminology

- **Solicited: Submitted at FDA's request, i.e. in response to a CR letter**
- **Unsolicited: Submitted on the applicant's own initiative, i.e., an amendment not requested by FDA**
  - **Delaying: Contains information not requested by FDA that is the result of changes to the RLD or USP monograph, changes to the RLD labeling, a REMS and REMS modification, or generic approval requirements reflected in CP responses**
  - **Nondelaying: Contains information not requested by FDA that is *not* the result of changes to the RLD or USP monograph, changes to the RLD labeling, a REMS and REMS modification, or generic approval requirements reflected in CP responses**
- **Administrative: Amendment that is routine in nature and does not require scientific review**

GDUFA Amendment Tiers: Tier 1

- 1st major and the 1st five minor solicited amendments
- All unsolicited delaying amendments
- Tier 1 Goal Dates:
  - 1st major amendment = 10-month goal
  - 1st – 3rd minor amendments = 3-month goal
  - 4th & 5th minor amendments = 6-month goal
  - Delaying amendments = 3-month goal
  - Any Tier 1 amendment requiring an inspection = 10-month goal

GDUFA Amendments Tiers: Tier 2

- All unsolicited nondelaying amendments
  - Any unsolicited, gratuitous change
  - Changes made not by the RLD
  - Changes not made at FDA's request
- Tier 2 Goal Dates:
  - All Tier 2 amendments = 12-month goal

GDUFA Amendment Tiers: Tier 3

- All solicited major amendments after the 1st major amendment
- All solicited minor amendments after the 5th minor amendment
- Tier 3 Goal Dates:
  - ≥ 2nd major amendment = NO GOAL
  - ≥ 6th minor amendment = NO GOAL

GDUFA Amendment Tiers: Administrative

- Neither Tier 1, Tier 2 nor Tier 3
- Will not impact the original review goal date
- Will not require scientific review

Summary of Tiers and Goals

	Solicited Amendment Goals	Unsolicited Amendment Goals
Tier 1	1st Major: 10 months 1st – 3rd Minor: 3 months* 4th – 5th Minor: 6 months*	Delaying: 3 months*
Tier 2	N/A	Nondelaying: 12 months
Tier 3	≥ 2nd Major: No goal ≥ 6th Minor: No goal	N/A

* 10 months if an inspection is required

Draft Guidance on Amendments & ECDs Under GDUFA

Draft Guidance Purpose & Goals

- **Assists applicants by explaining how GDUFA performance goals apply to amendments**
- **Incentivizes submissions of high-quality original applications**
- **Decreases the number of review cycles by demonstrating the penalty of extending or eliminating the review clock**

Defining Amendments

Guidance for Industry

Major, Minor, and Telephone Amendments to Abbreviated New Drug Applications

Comments and suggestions regarding this document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document contact Rita Hassall (301)827-5845

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
December 2001
Revision 2
OGD

Defining Amendments: Major

Major, Minor & Telephone Amendments (2001 guidance)	ANDA Submissions – Amendments & ECDs Under GDUFA (2014 draft)
Major amendments have the same review priority as original, unreviewed ANDAs and are reviewed in accordance with OGD's first in-first reviewed procedure	FDA review of a major amendment requires a **substantial expenditure of FDA resources.** Major amendments contain a substantial amount of new data or new information not previously submitted to or reviewed by FDA.

Defining Amendments: Minor

Major, Minor & Telephone Amendments (2001 guidance)	ANDA Submissions – Amendments & ECDs Under GDUFA (2014 draft)
Minor amendments have a higher priority than major amendments because they often mean an application is close to approval and should, therefore, be given priority. Except for those amendments that are classified as major or telephone, amendments will be designated as minor. Minor amendments often consist of deficiencies that are outside the control of the applicant or deficiencies that are more easily addressed than those in a major amendment.	FDA review of a minor amendment requires **fewer FDA resources than are necessary to review a major amendment but more than are necessary to review the information submitted in response to an easily correctable deficiency**.

Defining Amendments: ECD

Major, Minor & Telephone Amendments (2001 guidance)	ANDA Submissions – Amendments & ECDs Under GDUFA (2014 draft)
If an amendment would otherwise be classified as minor, but the deficiencies are of a limited number or complexity, it can be classified as a telephone amendment at the discretion of the reviewer's team leader. The applicant should provide a complete and satisfactory response within 10 calendar days of the call.	FDA review of information submitted in response to an easily correctable deficiency (ECD) will require only a **modest expenditure of FDA resources**. An applicant should be able to respond to an ECD quickly as the applicant should already possess or be able to quickly retrieve the information needed for an adequate response to an ECD.

Application of Amendment Goals

- **An amendment will only receive a performance goal date if the original ANDA or PAS being amended was submitted on or after 10/1/14**
  - **Ex.: No goal date will be assigned to an ANDA amendment if the original ANDA was submitted on September 30, 2014**
- **Performance goals are set from the date of the amendment's submission**

Application of Amendment Goals

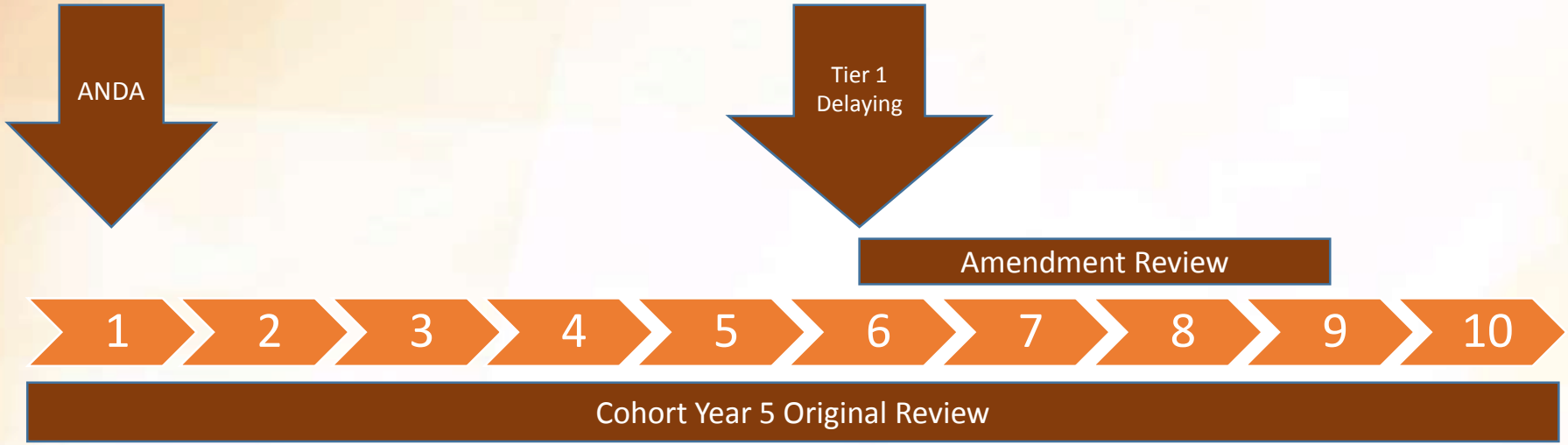
- **An amendment submitted before a CR letter is issued may adjust the goal date for the original ANDA**
- **Subsequent amendments submitted before a CR letter is issued also adjust the goal date for the original ANDA and are additive**

Application of Amendment Goals

An unsolicited amendment with a 12-month performance goal date submitted 4 months prior to the original goal date adds 8 months to the review clock

Application of Amendment Goals

A delaying amendment with a 3-month performance goal submitted 4 months prior to the original goal date does not change the goal date.

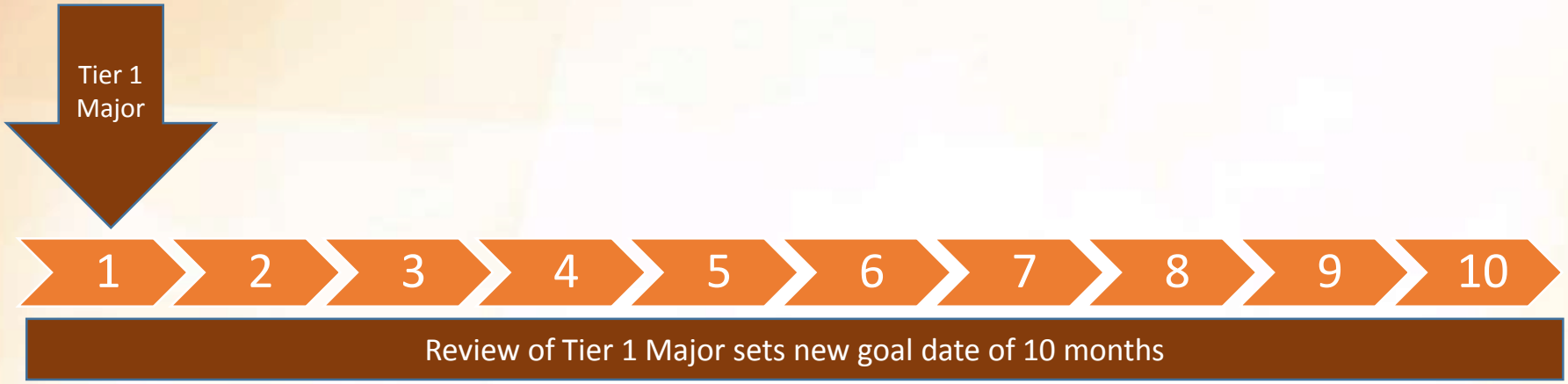


Application of Amendment Goals

- **Setting goal dates**
  - **An amendment submitted after a CR letter is issued sets a new goal date for the application**
  - **Subsequent amendments may adjust the goal date and are additive**

Application of Amendment Goals

A major amendment with a 10-month performance goal date submitted post-CR letter sets a new goal date for the application



Application of Amendment Goals

- **Losing goal dates**
  - **When an applicant submits a Tier 3 amendment, the ANDA will lose its goal date**
  - **Once the goal date is lost, no goal date will be set for any subsequent submission**

Application of Amendment Goals

- **Deferral**
  - **FDA has discretion to accept an unsolicited amendment submitted during the review cycle**
  - **FDA has discretion to defer review of an unsolicited amendment submitted during the review cycle**
  - **FDA will defer any unsolicited amendment submitted after the CR is issued and before the applicant submits the amendment in response to the CR letter**

Application of Amendment Goals

- **Requests for Final Approval**
  - **If no changes have been made to product or process since TA and applicable facilities maintain acceptable compliance status, request will be reviewed in ~3 months**
  - **If gratuitous changes have been made to product or process since TA, request will be classified as Tier 2 unsolicited nondelaying amendment and will be reviewed in 12 months**

Application of Amendment Goals

- **Expedited Applications**
  - **Certain submissions may be granted expedited review**
    - **MAPP 5240.3: Prioritization of the Review of Original ANDAs, Amendments & Supplements**
  - **Amendments to expedited submissions are subject to GDUFA performance goals**
  - **Review of an amendment to an expedited submission may be completed before the GDUFA performance goal**

Application of Amendment Goals

- **Classification**
  - **Based on the resources required to review the submission**
  - **Considers:**
    - **Type**
    - **Quantity**
    - **Complexity of information to be reviewed**

Application of Amendment Goals

- **Change in Classification**
  - **Major/Minor to Unsolicited**
  - **ECD to Minor/Unsolicited**
  - **Minor to Major for Overall Poor Quality**

Application of Amendment Goals

- **Change in Classification: Major/Minor to Unsolicited**
  - **If an applicant's CR amendment contains additional information unrelated to the CR deficiency *or* contains data beyond what was identified in the CR letter as necessary to correct the deficiency(ies),**
  - **Then FDA may classify the submission as an unsolicited amendment and adjust the performance goal**

Application of Amendment Goals

- **Change in Classification: ECD to Minor/Unsolicited**
  - **If a response to an ECD is not submitted within the time frame identified, then FDA may reissue the ECD as a minor deficiency in the next CR letter**
  - **If a response to an ECD contains unsolicited information, then FDA will classify the response as a Tier 2 unsolicited nondelaying amendment and adjust the performance goal**

Application of Amendment Goals

- **Change in Classification: Minor to Major for Overall Poor Quality**
  - **Scenario 1: FDA classification in the CR letter**
    - **If the review identifies multiple minor deficiencies of varying complexity, the review of which will require a substantial expenditure of FDA resources akin to review of a major amendment,**
    - **Then FDA may classify the response to the CR letter as a major amendment**

Application of Amendment Goals

- **Change in Classification: Minor to Major for Overall Poor Quality**
  - **Scenario 2: FDA changes classification upon review of the amendment**
    - **If a minor CR amendment is of such poor quality that FDA cannot review without substantial resources,**
    - **Then FDA may classify the submission as a major amendment**

Application of Amendment Goals

- **Inspections**
  - **FDA will determine an inspection is necessary and adjust the goal date when an applicant:**
    - **Submits its first minor amendment but the manufacturing site identified in the ANDA requires an inspection (10-month goal)**
    - **Submits its first minor amendment but in response to the CR letter, provides information on a facility being used for a new packaging line that requires an inspection (10-month goal)**
    - **Submits a Tier 2 nondelaying amendment that contains a new manufacturing site (12-month goal)**

Recommended Format for Submission

- A statement indicating whether the amendment is solicited or unsolicited
- Amendment classification
- Tier classification
- A statement indicating whether the amendment contains any manufacturing or facilities changes
- A listing of the disciplines to review the amendment
- A statement indicating whether expedited review is requested

Request for Reconsideration

- **Applicants may request reconsideration of:**
  - **Classification of CR amendment as a major**
  - **Change in amendment classification to a major**
- **If request is successful before the applicant submits their amendment, FDA will revise the classification and assign the appropriate performance goal upon submission**
- **If request is successful but the amendment has been submitted and review has started, FDA will not change or alter the goal date for that amendment, but the amendment count will be adjusted**

Status of the Draft Guidance

- Comments on the Guidance submitted to:
  - Guidance docket
  - Policy Development Public Meeting Docket
- Revisions to guidance underway
- Final guidance to issue this year

Questions?

Evaluation: surveymonkey.com/s/GDF-D2S9